

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants : Wai C. Wong, Yoon T. Jeon, T.G. Murali Dhar,  
and Charles Gluchowski

Serial No. : Not Yet Known

Filed : Herewith

For : IMIDAZOLE AND IMIDAZOLINE DERIVATIVES AND  
USES THEREOF

1185 Avenue of the Americas  
New York, New York 10036  
August 20, 2001

Assistant Commissioner of Patents  
Washington, D.C. 20231

Sir:

**PRELIMINARY AMENDMENT AND INFORMATION DISCLOSURE STATEMENT**

Please amend the subject application as follows:

**In the Specification:**

On page 1, line 3, please insert the following paragraph:

-- This application is a continuation of U.S. Serial No. 09/398,861, filed September 20, 1999, now allowed, a continuation of U.S. Serial No. 09/175,253, filed October 20, 1998, now U.S. Patent No. 6,093,727, issued July 25, 2000, a divisional of U.S. Serial No. 08/834,658, filed April 11, 1997, now U.S. Patent No. 5,866,579, issued February 2, 1999, the contents of which are hereby incorporated by reference into the subject application.--

**In the Claims:**

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A Marked-Up Version of Amended Claims showing the changes made is attached hereto as **EXHIBIT A**.

#### REMARKS

Claims 1 to 26 were pending in the subject application. By this Amendment, applicants have canceled claims 2, 5, 6, 9, 15, 16, 17, 18, 19, 20, 23 and 26 without prejudice or disclaimer, and amended claims 3, 4, 10, 11, 12, 14, 21 and 24. Accordingly, upon entry of this Amendment, claims 1, 3, 4, 7, 8, 10, 11, 12, 13, 14, 21, 22, 24 and 25 will be pending and under examination.

Applicants have amended claims 3, 4, 10, 11, 12, 14, 21 and 24 to change the claim dependency. Applicants maintain that the amendments to claims 3, 4, 10, 11, 12, 14, 21 and 24 raise no issue of new matter. Accordingly, applicants respectfully request that the Amendment be entered.

#### Information Disclosure Statement

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following references which are listed on the attached Form PTO-1449 (**EXHIBIT 1**). The following references were previously cited in connection with the prosecution of U.S. Serial Number 09/398,861 from which the subject application claims benefit under 35 U.S.C. §120. According to 37 C.F.R. §1.98(d), copies of patents or publications that were previously cited by, or submitted to, the Office in connection with such prior applications need not accompany the Information Disclosure Statement. Accordingly, copies of the following references are not attached to this Information Disclosure Statement:

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Please cancel claims 2, 5-6, 9, 15-20, 23 and 26 without prejudice to applicants' right to pursue the subject matter of these claims in a future continuation or divisional application.

Please amend the claims 3, 4, 10, 11, 12, 14, 21 and 24 as follows:

- 3. (Amended) The compound of claim 1, wherein the compound comprises the (+) enantiomer.--
- 4. (Amended) The compound of claim 1, wherein the compound comprises the (-) enantiomer.--
- 10. (Amended) The compound of claim 7, wherein p is at least 1 and at least one R<sub>3</sub> is methyl.--
- 11. (Amended) The compound of claim 7, wherein at least one R<sub>2</sub> is methyl.--
- 12. (Amended) The compound of claim 7, wherein at least one R<sub>2</sub> is bromo.--
- 14. (Amended) The compound of claim 7, wherein at least one R<sub>2</sub> is methyl or phenyl.--
- 21. (Amended) A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.--
- 24. (Amended) The method of claim 22, wherein the disorder is migraine headache, hypertension or glaucoma.--

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1. U.S. Patent No. 3,288,805, issued November 29, 1966, Berg, A.;
2. U.S. Patent No. 3,636,219, issued January 18, 1972, Culik, R. and Schneider, J. A.;
3. U.S. Patent No. 4,374,143, issued February 15, 1983, Dolman, H. et al.;
4. U.S. Patent No. 5,028,606, issued July 2, 1991, Venet, M. G., et al.;
5. U.S. Patent No. 5,663,189, issued September 2, 1997, Maurer, P. J., et al.;
6. PCT International Publication No. WO 92/14453, published September 3, 1992;
7. UK Patent Application GB 2206880, published January 18, 1989, Karjalainen, A. J., et al.;
8. Amemiya, Y., et al., "Synthesis and  $\alpha$ -Adrenergic Activities of 2- and 4-Substituted Imidazoline and Imidazole Analogues," J. Med. Chem. (1992) 35: 750-755;
9. Hong, S., et al., "A Structure-Activity Relationship Study of Benzylic Modifications of 4-[1-(1-Naphthyl)ethyl]-1H-imidazoles on  $\alpha_1$ - and  $\alpha_2$ -Adrenergic Receptors," J. Med. Chem. (1994) 37: 2328-2333;
10. von Kretzschmar, R., et al., "Zur Pharmakologie von N-(2-Imidazolin-2-yl)-N-(4-indanyl)amin (Indanazolin), einer neuen vasokonstriktorisch wirksamen Imidavalinverbindung," Arzneim.-Forsch./Drug Res. (1980) 30: 1746-60;

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11. Timmermans, P.B.M.W.M., et al., "Characterization of  $\alpha$ -adrenoceptor populations. Quantitative relationships between cardiovascular effects initiated at central and peripheral  $\alpha$ -adrenoceptors," J. Med. Chem. (1981) 24: 502-507; and
12. Wong, W. C., et al., "Design and Synthesis of Alpha<sub>2</sub> Adrenoceptor Agonists," 213th American Chemical Society Meeting, San Francisco, CA, April 13-17, 1997, Abstract No. 023, which was mailed to subscribers on March 8, 1997.

If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed \$490.00 fee for filing the subject application, is deemed necessary in connection with the filing of this Preliminary Amendment and Information Disclosure Statement. However, if an additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White  
Registration No. 28,678  
Attorney for Applicants  
Cooper & Dunham LLP  
1185 Ave of the Americas  
New York, New York 10036  
(212) 278-0400

Marked-up Version Of Amended Claims

Additions to the text are indicated by underlining; deletions are indicated by square brackets.

- 3. (Amended) The compound of claim 1 [or 2], wherein the compound comprises the (+) enantiomer.--
- 4. (Amended) The compound of claim 1 [or 2], wherein the compound comprises the (-) enantiomer.--
- 10. (Amended) The compound of claim [5] 7, wherein p is at least 1 and at least one R<sub>3</sub> is methyl.--
- 11. (Amended) The compound of claim [5] 7, wherein at least one R<sub>2</sub> is methyl.--
- 12. (Amended) The compound of claim [6] 7, wherein at least one R<sub>2</sub> is bromo.--
- 14. (Amended) The compound of claim [9] 7, wherein at least one R<sub>2</sub> is methyl or phenyl.--
- 21. (Amended) A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 [or 2] and a pharmaceutically acceptable carrier.--
- 24. (Amended) The method of claim 22 [or 23], wherein the disorder is migraine headache, hypertension or glaucoma.--

**EXHIBIT A**  
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